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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte PRAMOD K. SRIVASTAVA

Appeal 2008-3949
Application 09/657,722
Technology Center 1600

Decided:[1] March 20, 2009

Before DEMETRA J. MILLS, RICHARD M. LEBOVITZ, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

STATEMENT OF CASE

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for anticipation and obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

The following claims are representative.

19. A composition comprising a recovered population of peptides in admixture with a pharmaceutically acceptable non toxic carrier, wherein said recovered population of peptides is produced by a method comprising the steps of:

(a) purifying a population of stress protein-peptide complexes from mammalian tumor cells, wherein the stress protein is non covalently associated with the peptide in said complexes;

(b) releasing the peptides from said population of complexes to produce a released population of peptides; and

(c) recovering the released population of peptides.

22. The composition of claim 19 further comprising a cytokine.

23. The composition of claim 22 wherein said cytokine is selected from the group consisting of IL-lα, IL-I1β, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IFNα, IFNβ, IFNy, TNF ᵒᵛ, TNFβ, G-CSF, GM-CSF, and TGF-β.

Cited References

Berliner et al. (Berliner) US 5,210,076 May 11, 1993

Elfriede Noessner et al. (Noessner), "Tumor-Derived Heat Shock Protein 70 Peptide Complexes Are Cross-Presented by Human Dendritic Cells," 169 THE JOURNAL OF IMMUNOLOGY No. 10, 5424-32 (Nov. 15, 2002)

Grounds of Rejection

1. Claims 19, 22-31, and 52-55 are rejected under 35 U.S.C. § 112, first paragraph, for lack of written description.

2. Claim 19 is rejected under 35 U.S.C. § 102(b) as being anticipated by Berliner.

1. Claims 19, 22-31, and 52-55 are rejected under 35 U.S.C. § 112, first paragraph, for lack of written description.

ISSUE

The Examiner finds that the written description in this case has not set forth peptides recovered or isolated from the separation of stress protein-peptide complexes derived from tumors, and therefore the written description is not commensurate in scope with the claims which read on peptides in general isolated from tumors.

Appellant contends that to structurally identify each peptide within the large heterogeneous population of peptides that is associated with stress proteins is an impractical task, and that drafting the claim as a product-by-process claim avoids recitation of these structural features. (Br. 5.) For this reason, Appellant argues that the written description rejection is erroneous. (Br. 4.)

The issue is: Does the written description describe representative species of peptides recovered or isolated from the separation of stress protein-peptide complexes derived from tumors?

FINDINGS OF FACT

1. The claims of the instant invention are drawn to peptide compositions produced by the separation of a stress protein and its associated peptide. (Ans. 3.)

2. Although a stress protein-peptide complex can be determined and isolated, the claims as currently recited read on any protein fragment or polypeptide fragment that is derived from a mammalian tumor cell from which the complex was initially extracted. (Ans. 3-4.)

3. One of skill in the art would not be able to determine with any certainty what the composition comprises because the polypeptide and or peptides themselves have not been adequately described. (Ans. 4.)

4. There is a lack of characterization of the peptide or peptides, which makes up the composition, wherein detailed information regarding the structure or amino acid sequence of the peptide or peptides has not been provided in the Specification. (Ans. 4.)

5. Because the Specification has not described the structure and makeup of the peptides in the composition, the composition can be equivalent to any known composition wherein the composition comprises a peptide or protein fragment. (Ans. 4.)

6. The Specification, page 5, states that:

> The observation that stress proteins chaperone the antigenic peptides of the cells from which they are derived provides an approach for readily isolating antigenic peptides for a preselected tumor. Once isolated, the stress protein-peptide complexes are administered back to the animal from which they were derived in order to elicit an immune response against a preexisting tumor. Accordingly, this approach circumvents the necessity of isolating and characterizing specific tumor antigens

> and enables the artisan to readily prepare immunogenic compositions effective against a preselected tumor.
>
> In its broadest aspect, the invention provides a method for inhibiting proliferation of a preselected tumor in a mammal.

7. The term "stress protein," as used in the Specification means any cellular protein which satisfies the following criteria. It is a protein whose intracellular concentration increases when a cell is exposed to stressful stimuli, is capable of binding other proteins or peptides, and is capable of releasing the bound proteins or peptides in the presence of adenosine triphosphate (ATP) and/or low pH. Stressful stimuli include, but are not limited to, heat shock, nutrient deprivation, metabolic disruption, oxygen radicals, and infection with intracellular pathogens. (Spec. 6.)

8. The Specification provides examples for purification of Hsp 70, Hsp90 and gp96 heat shock protein complexes. (Spec. 19-24.)

9. The first stress proteins to be identified were the heat shock proteins (Hsp's). Hsp's typically are induced by a cell in response to heat shock. Three major families of mammalian Hsp's have been identified to date and include Hsp60, Hsp70 and Hsp90. The numbers reflect the approximate molecular weight of the stress proteins in kilodaltons. The members of each of the families are highly conserved. *See for example*, Bardwell et al., 81 PROC. NAT'L ACAD. SCI. 848-852 (1984); Hickey et al., 9 MOL. CELL BIOL. 2615-2626 (1989); and Jindal, 9 MOL. CELL BIOL. 2279-83 (1989). (Spec. 17-18.)

10. Members of the mammalian Hsp90 family identified to date include cytosolic Hsp90 (also known as Hsp83) and the endoplasmic reticulum

counterparts Hsp90 (also known as Hsp83), Hsp87, Grp94 (also known as ERp99) and gp96. *See, for example*, Gething et al., 355 NATURE 33-45 (1992). (Spec. 18.)

11. Members of the Hsp70 family identified to date include: cytosolic Hsp70 (also known as p73) and Hsc70 (also known as p72); the endoplasmic reticulum counterpart BiP (also known as Grp78); and the mitochondria1 counterpart Hsp 70 (also known as Grp75), 25 Gething et al., (1992). (Spec. 18.)

12. Members of the mammalian Hsp60 family have only been identified in the mitochondria, Gething et al. (1992). (Spec. 18.) It has been discovered that the Hsp30, Hsp60, Hsp70 and Hsp90 families are composed of proteins related to the stress proteins in amino acid sequence, for example, having greater than 35% amino acid identity, but whose expression levels are not altered by stressful stimuli. (Spec. 7, 19.)

13. Many members of Hsp families were found subsequently to be induced in response to other stressful stimuli including, but not limited to, nutrient deprivation, metabolic disruption, oxygen radicals, and infection with intracellular pathogens. *See, for example,* Welch, SCIENTIFIC AMERICAN 56-64 (May 1993); Young (1990), *supra*; Craig. 260 SCIENCE 1902-1903 (1993); Gething et a1. (1992), *supra*; and Lindquist et al. (1988). (Spec. 7.)

14. The major stress proteins accumulate to very high levels in stressed cells but occur at low to moderate levels in cells that have not been stressed. For example, the highly inducible mammalian Hsp70 is hardly detectable at normal temperatures but becomes one of the most actively synthesized

proteins in the cell upon heat shock (Welch et al., 101 J. CELL. BIOL.1198-1211 (1985)). (Spec. 17-18.)

15. The immunogenic stress protein-peptide complexes of the invention may include any complex containing a stress protein noncovalently associated with a peptide that is capable of inducing an immune response in a mammal. Preferred complexes include, but are not limited to, Bsp70-peptide, Hsp90 peptide and gp96 peptide complexes. For example, the mammalian stress protein gp96 which is the endoplasmic reticulum counterpart of the cytosolic Hsp90 may be used in the practice of the instant invention. (Spec. 19.)

PRINCIPLES OF LAW

"The burden of showing that the claimed invention is not described in the application rests on the PTO in the first instance." *In re Edwards,* 568 F.2d 1349, 1354 (CCPA 1978). Compliance with the written description requirement is determined by whether the disclosure shows possession to a person of ordinary skill in the art. *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000).

A written description of an invention involving a chemical genus, like a description of a chemical genus, "requires a precise definition, such as by structure, formula, [or] chemical name," of the claimed subject matter sufficient to distinguish it from other materials. *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993). While "examples explicitly covering the full scope of the claim language" is not typically required, a sufficient number of representative species must be included "to demonstrate that the [applicant]

possesses the full scope of the invention." *LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005). This requirement applies not only to compositions of matter, but to methods as well. *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 926 (Fed. Cir. 2004). However, the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter. *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005).

"Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods." *University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 926 (Fed. Cir. 2004).

ANALYSIS

The Examiner argues that the claims of the instant invention are drawn to peptide compositions derived from the separation of a stress protein and its associated peptide. (Ans. 3.) The Examiner argues that although the stress protein-peptide complex can be determined and isolated, the claims as currently recited read on any protein fragment or polypeptide fragment that is derived from a tumor cell from which the complex was

initially extracted. (Ans. 3-4.) Thus, the Examiner concludes that one of skill in the art would not be able to determine with any certainty what the composition comprises because the polypeptide and or peptides themselves have not been adequately described. (Ans. 4.) The Examiner finds that there is a lack of characterization of the peptide or peptides, which makes up the composition, wherein detailed information regarding the structure or amino acid sequence of the peptide or peptides has not been provided in the Specification. (Ans. 4.) The Examiner concludes that because the Specification has not described the structure and makeup of the peptides in the composition, it can be equivalent to any known composition wherein the composition comprises a peptide or protein fragment. (Ans. 4.)

Appellant contends that to structurally identify each peptide within the large heterogeneous population of peptides that is associated with stress proteins is an impractical task, and that drafting the claim as a product-by-process claim avoids recitation of these structural features. (Br. 5.) For this reason, Appellant argues that the written description rejection is erroneous. (Br. 4.)

We are not persuaded by Appellant's argument. During prosecution claims are to be given their broadest reasonable interpretation. *In re Buszard*, 504 F.3d 1364, 1366-67 (Fed. Cir. 2007). As the Examiner rightfully recognized, the pending claims are broad and read on any protein fragment or polypeptide fragment that is derived from a tumor cell from which the population of stress protein-peptide complexes was initially extracted. "[E]ven though product-by-process claims are limited by and

defined by the process, determination of patentability is based on the product itself." *In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985).

> The patentability of a product does not depend on its method of production. If the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.

Id. (citations omitted). *See also Atlantic Thermoplastics Co., Inc. v. Faytex Corp.,* 970 F.2d 834, 843-47 (Fed. Cir. 1992).

Appellant argues that *Atlantic Thermoplastics* and other cases have held that product-by-process claims are an exception to the general rule requiring claims to define products in terms of structural characteristics. (Br. 4-5.) Appellant's arguments are not persuasive. We acknowledge that product-by-process claims are an acceptable claim drafting format and no issue is presented by Appellant's use of this claim form. The issue before us is whether the written description supports the present claim scope with sufficient representative examples covering the full scope of the product-by-process claim. Appellant has not contested the scope of the claim as interpreted by the Examiner. Nor has the Appellant presented case law relevant to the written description issue and product-by-process claims.

In *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927 (Fed. Cir. 2004), the Federal Circuit found that certain process claims lacked descriptive support. Although *Rochester* did not involve product-by-process claims, *Rochester* would reasonably appear to be pertinent to product-by-process claims. In *Rochester*, the court held that the disclosure of screening assays and general classes of compounds was not adequate to describe

compounds having the desired activity: without disclosure of which peptides, polynucleotides, or small organic molecules have the desired characteristic, the claims were not adequately described. *See University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927 (Fed. Cir. 2004) ("As pointed out by the district court, however, the '850 patent does not disclose just 'which "peptides, polynucleotides, and small organic molecules" have the desired characteristic of selectively inhibiting PGHS-2.' … Without such disclosure, the claimed methods cannot be said to have been described.").

In our opinion, Appellant's product-by-process argument exalts form over substance. If simply placing any process claim into a "product by process" format is sufficient to avoid concerns regarding the written description requirement, then the University of Rochester could have simply evaded the written description issue by rewriting the method claims into a "product by process" format. *Rochester* notes that "[r]egardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds." *Rochester*, 358 F.3d at 927. We conclude that the same rule of written description should apply to "product by process" claims as would apply to products *per se* or method claims. We find that the instant Specification fails to provide a description of the claimed compounds which permits the artisan to distinguish infringing from non-infringing compounds (FF 2, 4, 5).

We do not find that Appellant has disclosed a representative number of species falling within the scope of the pending claims. While the

Specification exemplifies complexes with Hsp60, Hsp70 and Hsp90, many other peptides and fragments are encompassed by the claims, without further limitation. The determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter. *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005). In the present case, Appellant has not shown that these three species of peptide complexes exemplified in the Specification are representative of the large group of peptides encompassed by the claims, or that the technology and claimed subject matter is such that a general description is sufficient to support the pending claim scope.

One of skill in the art would not be able to determine with any certainty what the composition comprises because the polypeptide and or peptides themselves have not been adequately described.

We affirm the written description rejection.

2. Claim 19 is rejected under 35 U.S.C. § 102(b) as being anticipated by Berliner.

CLAIM INTERPRETATION

During prosecution claims are to be given their broadest reasonable interpretation. *In re Buszard*, 504 F.3d 1364, 1366-67 (Fed. Cir. 2007).

Claim 19 recites a "composition comprising a recovered population of peptides." The claim does not specify whether the population is homogenous or heterogeneous population of peptides. Giving the claim its broadest reasonable interpretation, we interpret claim 19 as encompassing both homogenous or heterogeneous populations of peptides.

ISSUE

The Examiner contends that Berliner discloses and isolated tyrosinase protein, and Noessner evidences that tyrosinase protein can be associated with HSP70 protein forming a complex. (Ans. 4.)

Appellant contends that Berliner does not disclose or suggest the isolation of a population of peptides noncovalently associated with a stress protein in a mammalian tumor cell, and that Berliner does not disclose a heterogeneous population of peptides, as claimed. (Br. 7.)

The issue is: Does Berliner disclose a composition comprising a recovered population of peptides in admixture with a pharmaceutically acceptable non toxic carrier?

PRINCIPLES OF LAW

"A rejection for anticipation under section 102 requires that each and every limitation of the claimed invention be disclosed in a single prior art reference." *In re Paulsen*, 30 F.3d 1475, 1478-79 (Fed. Cir. 1994); *Karsten Mfg. Corp. v. Cleveland Golf Co.*, 242 F.3d 1376, 1383 (Fed. Cir. 2001). "[E]ven though product-by-process claims are limited by and defined by the

process, determination of patentability is based on the product itself." *In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985).

> The patentability of a product does not depend on its method of production. If the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.

Id. (citations omitted). *See also Atlantic Thermoplastics Co., Inc. v. Faytex Corp.,* 970 F.2d 834, 843-47 (Fed. Cir. 1992).

ANALYSIS

The Examiner argues that the claim is drawn to a composition comprising a recovered population of peptides admixed with a pharmaceutically acceptable non-toxic carrier. (Ans. 4.) The Examiner finds that Berliner discloses a tyrosinase protein wherein the said protein is found in a compound comprising a pharmaceutically acceptable carrier. As evidenced by Noessner, tyrosinase is a peptide which can be associated with a HSP70 protein, thereby forming a complex. (Ans. 4.) Therefore, because the claimed peptide product is already known, the process by which the product is made does not carry any patentable weight. *In re Thorpe,* 777 F.2d 695, 698 (Fed. Cir. 1985). (Ans. 4.)

The Examiner also argues that the claim encompasses a homogenous population of peptides. (Ans. 10.) Consistent with the claim interpretation herein, we find that claim 19 encompasses both a heterogeneous and homogenous populations of peptides, and thus claim 19 is not limited to a heterogenous peptide population as argued by Appellant. Appellant argues

that the claimed invention relates to a population of peptides recovered from stress proteins and that Berliner does not disclose such a population. (Br. 7-8.) We decline to read the word "heterogenous" into the claim. "[L]imitations are not to be read into the claims from the specification." *In re Van Geuns*, 988 F.2d 1181, 1184 (Fed. Cir. 1993) (*citing In re Zletz*, 893 F.2d 319, 321 (Fed. Cir. 1989)).

We further agree with the Examiner that the prior art teaches a peptide, tyrosinase, that is capable of binding to HSP in a noncovalent fashion. We agree that the Specification has not provided any indication that the method of producing the population of peptides imparts any structurally distinct aspect. Since the product is taught in the prior art and by a specific sequence, and the Specification fails to teach any specific structural distinction between the prior art peptides and those claimed, the claims are anticipated. (Ans. 10.)

In sum, Noessner discloses that tyrosinase complexes with HSP70. Berliner discloses the purification of a homogenous population of tyrosinase. Thus, Berliner discloses a peptide as claimed. The anticipation rejection is affirmed.

SUMMARY

The written description rejection is affirmed. The anticipation rejection is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

clj

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